# Effectiveness And Cost-Effectiveness Of Cognitive Behaviour Therapy And Short-Term Psychoanalytic Psychotherapy Compared With Brief Psychosocial Intervention In Maintaining Reduced Depressive Symptoms 12 months after end of treatment in Adolescents with Unipolar Major Depression (IMPACT): A Pragmatic Superiority Randomised Controlled Trial

Ian M Goodyer, Shirley Reynolds, Barbara Barrett, Sarah Byford, Bernadka Dubicka, Jonathan Hill, Fiona Holland, Raphael Kelvin, Nick Midgley, Chris Roberts, Rob Senior, Mary Target, Barry Widmer, Paul Wilkinson, Peter Fonagy

**Summary**

**Background** Psychological treatments for adolescents with unipolar major depressive disorder (MDD) are associated with diagnostic remission within 28 weeks in 65%-70% of cases. It is not known however whether a particular psychological treatment that is effective for the acute episode results in a sustained recovery, thereby reducing relapse risk, in the year following end of treatment.
**Methods** In this observer blind, parallel group, pragmatic superiority randomised controlled trial (IMPACT), we recruited adolescent patients (11-17 years) with a DSM IV major depressive episode from 15 NHS CAMHS clinics in England. Participants were randomly assigned to one of two established treatments, cognitive behaviour therapy (CBT) or short-term psychoanalytic therapy (STPP), which were compared to a reference brief psychological intervention (BPI). Treatment allocation was carried out by the trial coordinator using stochastic minimization controlling for age, gender and self-reported depression sum score. The patients were followed up and reassessed at five planned time points from randomisation. The primary outcome was self-reported depression symptoms obtained at the notional 36,52 and 86 week post randomisation assessment. The primary analysis was based on intention to treat. The trial is registered with Current Controlled Trials, ISRCTN83033550.
**Findings** Between June 29th 2010 and January 17th 2013 we assessed 557 patients of whom 87 were excluded as not meeting eligibility criteria, 5 withdrew after treatment allocation and 465 were included. These were randomly assigned to BPI (n=155), CBT (n=154) and STPP (n=156) respectively. Treatment fidelity and differentiation were established between the three interventions. The median number of treatment sessions was significantly different (BPI = 6; CBT = 9, STPP = 11, Kruskal-Wallis rank test p<0·001) but there was no difference in the average duration of treatment in weeks between the groups (BPI 27·5 (sd 21·5), CBT 24·9 (sd17·7), STPP 27·9 (sd16·8), Kruskal Wallis p= 0·238). Of the 465 who entered the study 392 (84%) had available data for primary analysis by end of follow up. There were no significant differences between STPP and CBT in reducing depressive symptoms by end of study (treatment effect by final follow up = 0·578, 95% CI, -2·948 to 4.104, p= 0·748) nor were there any superiority effects for these two treatments (CBT+STPP) compared to BPI (treatment effect by final follow up = -1·898, 95% CI, -4·922- 1·126, p= 0·219). By the notional 86 week final assessment there was no significant difference in the mean depressive score between treatment groups. There was an average 49-52% reduction in symptoms 12 months after the end of therapy. At end of study, 221 (77%) of the 286 consenting to interview, were in diagnostic remission. Physical adverse effects (breathing problems, sleep disturbances, drowsiness/tiredness, nausea, sweating, restless/overactive) were no different between the groups. Prescribing of an SSRI during treatment or in the post treatment follow-up period did not differ between the treatment arms and so did not mediate the outcome. The proportion of patients who reported suicide attempts or non suicidal self injury by end of study was not increased over the baseline assessments nor associated with SSRI prescribing over the study. There were no differences in total costs or quality of life scores between treatment groups.
**Interpretation** All three psychological therapies are associated with maintaining reduced depressive symptoms up to a year after the end of treatment. STPP is as effective as CBT and together with BPI offers additional patient choice for psychological therapy, alongside CBT, for moderately to severely depressed adolescents attending routine specialist CAMHS.
**Funding** National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme, and the Department of Health.

## Research in context

### Evidence before this study

Unipolar major depression emerges with the highest incidence risk rate in the second decade of life affecting a substantial proportion of the adolescent population worldwide. There is good evidence for psychological treatments being associated with clinical remission in some 70% of cases. In contrast data are lacking on whether one or more of the available therapies is associated with maintaining reduced depressive symptoms a year after the end of treatment. This is a non-trivial issue because lowered depressive symptoms below a clinical threshold 12 months after end of treatment is associated with reduced risk for diagnostic relapse into the adult years. A literature search was carried out of the USA National Library of Medicine (http://www.ncbi.nlm.nih.gov/pubmed/) database from 1st August 1990 to 31st August 2016 using the search terms adolescence, depression, psychological treatments, randomised controlled trials, remission, relapse, relapse prevention and adverse effects. The search found, 3 trials on school population based interventions a small (n=43) feasibility study for a social media intervention for relapse prevention using recovered depressed patients and a Cochrane data base review on preventing relapse in depressed children and adolescents. Currently there are no identified psychological treatments that can be recommend as effective in maintaining reduced depressive symptoms in the year following successful treatment.

### Added value of this study

This trial showed that there were no superiority effects for either of two established psychological treatments, short term psychoanalytic psychotherapy (STPP) and Cognitive Behaviour Therapy (CBT), delivered by highly trained therapists over 28 and 20 weeks respectively, against a reference brief psychosocial intervention delivered over 12 weeks by child and adolescent psychiatrists and mental health nurses. All three psychological treatments were associated with an average 49-52% reduction in depression symptoms a year after treatment. Prescribing an SSRI during therapy or follow-up as per NICE guidelines did not differ between the treatment arms and so did not mediate the outcome. Suicide attempts and self harm attempts over the follow up period were lower than at baseline as were physical side effects. Furthermore there were no differences in total costs or quality of life scores between treatment groups by end of study. To our knowledge this is the only high-quality, fully powered superiority and cost-effectiveness study addressing the medium term effects and costs of psychological treatments on maintaining reduced depressive symptoms 12 months after treatment.

### Implications of all the available evidence

All three treatments are associated with maintaining reduced depressive symptoms up to a year after the end of treatment. STPP is as effective as CBT and together with BPI offers an additional patient choice for psychological therapy, alongside CBT, for moderately to severely depressed adolescents attending routine specialist CAMHS.

**Word Count: 4488**

## Introduction

Unipolar major depression (MD) is a significant mental illness affecting a substantial proportion of the adolescent population worldwide.[1] Although there is evidence for the effectiveness of treatments in the short-term, data is lacking on whether one or more of the available psychological treatments is also able to maintain reduced depressive symptoms a year after the end of therapy. [2 3] This is a non-trivial issue because maintaining lowered depressive symptoms below a clinical threshold level reduces the risk for diagnostic relapse into the adult years.[4] Cognitive behaviour therapy (CBT) offer plausible long-term benefits for depressed adolescents and are recommended as such by NICE.[5] Short-term psychoanalytic psychotherapy (STPP) alos shows preliminary promise as a therapy for depressed adolescents. CBT has established clinical effectiveness and relapse prevention and STPP has evidence for clinical effectiveness in depressed adults comparable to CBT and in adolescents some evidence for clinical effectiveness .[6, 7,8,9] In this study we tested a primary hypothesis that these two psychological therapies (CBT and STPP) would be significantly more likely to maintain reduced depressive symptoms at 86 weeks post randomisation (approximating 52 weeks post treatment) when compared to a reference brief psychosocial intervention (BPI). The reference intervention has evolved as a manualised form of specialist clinical care (SCC) used as the brief psychosocial intervention as usual in a previous trial of depressed adolescents. In that study the findings suggested that this intervention maybe clinical effective (see appendix i). [10]

## Method

### Study design and participants

The "Improving Mood with Psychoanalytic and Cognitive Therapies" (IMPACT) study is a multicentre, pragmatic, superiority, parallel, and single blind randomised controlled trial. The study was conducted with adolescents with an episode of DSM IV major unipolar depression referred to routine Child and Adolescent Mental Health Services (CAMHS) clinics in England.[10,11] In the UK National Health Service, adolescents who do not respond to community based treatments may be sent to specialist CAMHS outpatients. Therefore the depressed adolescents entered into this randomised controlled trial were patients with high numbers of symptoms and concurrent personal impairments. The study design and procedures are presented in full in the published trial protocol.[12]

The study was run in three regions of England: East Anglia, a largely rural area of three million people with four urban areas each containing approximately 100,000 people; North London, a densely populated urban area with around four million people; and the North West of England, covering approximately four million people of whom about one million live in rural surroundings and three million living in the City of Manchester. There were 15 participating routine CAMHS clinics (five in each region). Patients were included from either sex aged 11 through 17 years who met DSM-IV unipolar major depressive disorder diagnosis (MDD). [12] Exclusion criteria were generalised learning difficulties, pervasive developmental disorder, pregnancy, currently taking another medication that may interact with an SSRI, current substance or alcohol abuse, previously completed one of the study treatments, a primary diagnosis of Bipolar Disorder, Schizophrenia or Eating Disorders. No other exclusions were made. The study was approved by the UK National Health Service NRES Committee East of England - Cambridge Central (09/H0308/137) and local NHS provider trusts. The trial was conducted and reported in accordance with CONSORT guidelines.[13]

### Randomisation and Masking

Treatment allocation was carried out by the trial coordinator using stochastic minimization controlling for age (11-13;14-15;16-17 years), gender, self-reported depression sum score (< =29; 30-39;40-49; >=50)[8] and region (East Anglia; North London; North West England) using an on-line randomization service (www.sealedenvelope.com). In view of the nature of the interventions, patients and clinicians were aware of treatment allocations.

### Measures

The primary outcome measure was the current level of depressive symptoms as recorded by the self-reported Mood and Feelings Questionnaire (MFQ). [14] Secondary outcomes were self-reported sum scores on the Revised Children's Manifest Anxiety Scale (RMAS), the revised Leyton Obsessional Inventory (LOI) for adolescents, and the Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA) a measure of overall current psychosocial impairment. [15, 16, 17] A brief self-reported antisocial behaviour checklist based on DSM IV conduct disorder criteria was used as a binary (none, one or more) measure of antisocial behavioural symptoms. The presence of major depressive episode using the Kiddie-Schedule for Affective Disorder and Schizophrenia (K-SADS-PL) was also measured over time.[18] The study was not however powered to test a specific diagnosis hypothesis. Two additional clinical measures were added: the Columbia Suicide Inventory [29]; the self-report Risk and Self Harm Inventory. [19] Treatment fidelity and differentiation were assessed using the Comparative Psychotherapy Process Scale (CPPS) and (for BPI fidelity) the Brief Psychosocial Intervention Scale (BPI-S) (appendix i).[21] Economic measures included the Child and Adolescent Service Use Schedule (CA-SUS), for collection of service and other resource use, and the EQ-5D-3L™ measure of health-related quality of life, used to calculate quality-adjusted life years (QALYs).[22,23]

### Procedures

All treatments were manualised and a description of the treatment manuals including theoretical and operational differences, are given in the online appendix (appendix i). Treatment manuals are also posted on a weblink (dev.psychiatry.cam.ac.uk/projects/). A total of 63 therapists delivered BPI, 44 delivered CBT and 38 STPP. Short-term psychoanalytic psychotherapy (STPP) is a 28-session model, with parents or carers being offered up to seven additional sessions by a separate parent worker. STPP was a planned programme of 28 sessions over 30 weeks. The techniques of STPP are based on close and detailed observation of the relationship the child or young person makes with their therapist. The therapist introduces the therapeutic task to the young person as one of understanding feelings and difficulties in their

life. The therapist is non-judgemental and enquiring and conveys the value of self-understanding. STPP has previously been reliably and effectively delivered.[9] STPP therapists were CAMHS clinicians with a psychoanalytic child and adolescent psychotherapy training. CBT in this trial is based on the classical form originally developed for adults with depression .[24] It was adapted to include parental involvement, focused on engagement in therapy, and highlighted the use of behavioural techniques. The focus of CBT is to identify the behaviours and information processing biases that maintain depression and low mood and to amend these through a process of collaborative empiricism between the therapist and client. CBT was a planned programmer of up to 20 sessions over 30 weeks. CBT therapists were routine CAMHS clinicians and were either clinical psychologists, or other clinicians who had received post qualification training in CBT. BPI was formulated and developed from the routine specialist clinical care delivered in the Adolescent Depression Antidepressants and Psychotherapy trial (ADAPT).[9] The emphasis in the BPI programme is on the importance of psychoeducation about depression together with action oriented, goal-focused and interpersonal activities as therapeutic strategies. Neither self-understanding nor cognition change are considered. BPI was derived from a practice based specialist clinical care package used in the ADAPT study and reformulated for this investigation based on that trial experience. BPI consists of 12 individual sessions including up to four family/marital sessions delivered over 20 weeks. The BPI therapists were drawn from routine CAMHS services, the majority (85%, 53) were psychiatrists who had passed postgraduate general training (obtained their membership of the Royal College of Psychiatrists) and subsequently entered specialist CAMHS psychiatry training as well as consultants. For all three arms, liaison with external agencies and personnel e.g. teachers, social care, and peer group were commonly undertaken. All therapy sessions were audiotaped and a random sample of 232 tapes (76 CBT tapes, 81 STPP tapes and 75 BPI tapes) were selected and rated using the CPPS and the BPI-S rating scales. Independent raters rated each treatment session from the three treatment modalities to assess treatment fidelity for the CBT, BPI, and STPP arms (Appendix i). Following NICE guidelines fluoxetine could be added where clinicians judged that combination therapy may accelerate the time to remission.[5] A test dose of 10 mg was given for 48 hours followed by 20 mg as a single dose. If there was no improvement within two to four weeks the dose could be adjusted upwards to 60 mg maximum.

**Study Hypotheses** The investigation tested a primary superiority hypothesis that:

i) Compared to patients randomised to BPI, patients who receive either STPP or CBT will be superior at maintaining significantly lower self-reported depressive symptoms by end of study.

Since we evaluated two psychological therapies, CBT and STPP, against a reference brief psychosocial intervention we first determined if there were differences between them. Therefore we first tested whether CBT was inferior to STPP for the same outcomes.

In previous studies of psychological treatment with depressed adolescents, anxiety symptoms have been reduced even where depressive symptoms have not. Therefore we tested a secondary hypothesis that:

ii) Compared to those randomised to BPI, patients who received CBT or STPP will be superior at maintaining significantly lower self-reported anxiety symptoms but significantly higher research interviewer-evaluated psychosocial function by end of study.

Finally a cost-effectiveness hypothesis tested:

iii) Whether the additional cost of the psychological treatments, CBT and STPP, can be justified by improvements in clinical effectiveness and/or decreased use of health and social care services compared to BPI by 86 weeks follow up.

**Sample Size and Statistical Analysis**
A 2.5% two-sided significance level was used for calculating sample size and interpretation of analyses. Clustering of patients by therapist was assumed. Five points on the MFQ was taken to represent a clinically important difference for assessment of superiority, which corresponds to a one point improvement on five of the 33 items of MFQ. It is a standardize effect size of 0·34 (small to medium) and corresponds to non-overlap between treatments of approximately 25%. Data from the ADAPT trial gave an estimate of the SD of the primary outcome measure (14·6) and correlation between baseline and follow-up (0·41).[10] The study planned for a recruited sample size of 540. Assuming 90%, (n=486) follow-up and a 2·5% significance level to account for multiplicity, the power for the comparison of CBT with STPP was 84% if the ICC was zero, 76% for an ICC of 0·025, and 69% if it was as large as 0·05.[24] For the comparison of the established

treatments (CBT+STPP) with BPI the power was 93%, 88%, and 82% for an ICC of 0·0, 0·025, or 0·05 respectively. [25]

The intention-to-treat principle was applied for all analyses subject to the availability of data. STATA 12.0 was used for all analyses. The objective was to establish the outcomes following end of treatment, therefore only data from 36, 52 and 86 week assessments were used for the primary analyses. The marginal treatment effect was estimated using a linear mixed model with a random effect for therapist, patient and slope. To prevent bias due to assessments being delayed, time since randomisation was used as a continuous variable in a longitudinal mixed model(see appendix ii, section 6.3). MDD diagnoses (present/absent) was analysed using a logistic GEE model over the same time period. All analyses included fixed covariates pre-specified at baseline MFQ, RMAS, LOI, ABQ scores, treatment allocation, region, sex, age at randomisation, co-morbid behaviour disorder, prescription of SSRI before trial entry (see statistical analysis plan published in appendix iii and https://figshare.com/articles/IMPACT_Statistical_Analysis_Plan/3423109).

Full methods and results of the economic evaluation are reported in the online data (appendix iii) and also available on our weblink (dev.psychiatry.cam.ac.uk/projects/). Methods have been applied in a previous trial.[26] In brief, cost-effectiveness was explored at the 86 week follow up with outcomes expressed as quality adjusted life years (QALYs) and costs considered from a service perspective (health, social care, and education). Unit costs were for the financial year 2011/12 and costs and QALYs were discounted at a rate of 3·5% as recommended by NICE.[27] Differences in mean costs were tested using linear regression models with the validity of the results confirmed using bias-corrected, non-parametric bootstrapping (5000 re-samples).[25] For the cost-effectiveness analysis, incremental cost-effectiveness ratios (ICERS) were calculated (the difference in mean cost divided by the difference in mean effect) and uncertainty was explored using cost-effectiveness acceptability curves (CEACs), which show the probability that each of the treatments is the optimal choice, for a range of possible values of willingness to pay for additional QALYs.[28] All economic analyses were adjusted for the pre-specified covariates as well as baseline utility and cost, as appropriate. Complete case analysis was used, with the impact of missing data and the impact of sessions offered but not attended explored in sensitivity analyses.

**Role of the funding source**
The funder of the study had no role in study design, data collection, data analysis, interpretation of data, or writing of the paper. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

**Results**
Between June 29th 2010 and January 17th 2013 we assessed 557 patients from 15 NHS CAMHS teams, five from each regional centre in England. Of these 87 were excluded and 470 were recruited (see Figure 1). The 470 participants were randomised but five withdrew and requested data be deleted (3 BPI, 1 CBT and 1 STPP). The remaining 465 participants were randomised to BPI (n=155), CBT (n=154), and STPP (n=156), respectively. The regional recruitment was: East Anglia 40%, n=185, North West 33%, n=153 and North London 27%, n=127. Completed primary outcome measure (MFQ) at each notional time point was: baseline 465(100%); 6 week=310 (67%), 12 week= 326 (70%), 36week = 318 (68%), 52 week = 326 (70%), 86 week = 353 (76%). A total of 392 (392/465, 84%) participants were retained and had data over the follow up period and used in the primary analysis (BPI, 132 (85%) of 155, CBT, 133 (86%) of 154, STPP, 127 (81%) of 156). Of these 39 (10.0%) had one, 90 (23.0%) and 263 (67%) had 3 MFQ scores. The pattern of collected secondary outcomes was similar between treatment groups. The data available was within the margins suggested by the power calculation. Baseline characteristics were balanced between treatment groups (see Table 1). There were no significant differences between treatment groups.

Figure 1 about here
Table 1 about here

The full depression symptom profile at baseline is shown in appendix 2 (table A1). The mean number of symptoms was: BPI= 8·4, CBT=8·7, STPP= 8·3. The most prevalent symptom was sleep disturbance (92%, 427) followed by depressed mood (84%, 390). Psychotic symptoms were uncommon (10%, 48) but current suicidal ideas (61%, 284) and lifetime suicide attempts were notable (38%, 177). There were no symptom prevalence differences between the treatment groups. A total of 225 (48%) were concurrently comorbid with 71(46%,) for BPI, 80(52%) for CBT and 73(47%) for STPP groups(appendix 2, table A2). Overall 134 (29%) reported one, 60 (13%) two and 31(7%) 3 or more non-depressive comorbidities with no marked

differences between the groups. Non-suicidal self injury (NSSI) in the last 2 weeks was reported by 85 (18·3%) of the patients: BPI = 26, (17%), CBT= 25 (16%), STPP= 34 (22%). Lifetime NSSI was reported by 246 (53%) participants: BPI= 87 (56%), CBT= 75 (49%), STPP= 84 (54%).

**Uptake and duration of trial therapies**
The numbers of patients who started therapy were: BPI= 138 of 155 (89%), CBT= 133 of 154 (86%), STPP=133 of 156 (85%) (appendix, table A3). The proportion that initiated treatment did not differ by arm ($\chi_2^2$p=0·203). The number of individual treatment sessions given per group was briefer than planned but significantly different: (median) BPI= 6, CBT= 9, STPP= 11 (Kruskal-Wallis rank test p<0.001). Of those patients randomised to BPI 24 , (17%) had more sessions than the manual specified, compared to 5 (3%) for CBT and 3 ( 2% ) for STPP. Average duration of therapy between treatment groups was not significantly different: BPI 27·5 (sd 21·5), CBT 24·9 (sd17·7) and STPP 27·9 (sd16·8) weeks (Kruskal Wallis p= 0·238).

**Treatment fidelity and differentiation**
Overall 81% of BPI , 80% of STPP and 74% of CBT sessions met criteria. Treatment differentiation was good: the mean cognitive-behavioural (CB) sub-scale score on the CPPS was 1·91 higher for CBT than STPP sessions (95% CI 1·73 to 2·09,p <0·0001). The mean psychodynamic-interpersonal (PI) sub-scale score on the CPPS was 1·18 higher for STPP than CBT sessions (95% CI 1·01 to 1·3, p <0·0001). BPI sessions had a significantly lower CB sub-scale mean than CBT (mean diff. = -0·93, 95% CI -1·12 to -0·75, p<0·0001) and a significantly lower PI sub-scale mean than STPP (mean diff. =-1·30, 95% CI -1·48 to -1·11, p<0·0001).

**Medication**
We noted that 89 (19%) patients were receiving an SSRI prior to randomisation: BPI= 29 (19%), CBT= 32 (21%), STPP= 28 (18%) . By the end of study the proportion of patients in each arm who reported having received an SSRI at any time over the course of the trial (randomisation through to 86 weeks) per treatment group were: 56 (41%) for BPI, 55 (40%) for CBT, and 50 (36%) for STPP ($\chi_2^2$ $p$=0.729) (appendix ii table A4).
.
**Clinical results**
Table 2 gives summary statistics and the treatment effect estimates from the Linear Mixed Model. To investigate non-response a logistic GEE model was fitted to an indicator variable for missing primary outcome data. Behavioural disorder at baseline was found to predict non-response. As this was not a pre-specified baseline covariates it was added to all models of outcome to support the missing at random assumption. Time from randomisation to assessment and estimates of the main effect and time with treatment interaction are given in appendix ii table A5 and A6 respectively.

Table 2 about here

For the primary outcome at end of study there were no significant differences between STPP and CBT and none for combined treatments (CBT+STPP) compared to BPI. With a lower score representing improved outcome there was a larger difference in favour of combined established treatments of -3·234 (95% C.I. -6.611 to 0.143) at 36 week and -2·806 (-5.790 to 0.177) at 52 week assessments but these reductions were not statistically significant, less than the five units pre-specified as a clinically meaningful difference and not accompanied by differences in psychosocial impairment. The secondary outcomes revealed a significant reduction in anxiety and obsessional symptoms for the established therapies as compared to reference therapy at 36 week only. The intra-cluster correlation coefficient (ICC) for therapist was calculated as the proportion of the random intercept variance and was negligible ($<10^{-7}$) for all of the models. Study power was therefore at the upper end of the range as the sample size calculation considered a range of values of the ICC from 0 to 0.05.

The two secondary binary outcomes were the proportion of patients who i) self reported none or one or more antisocial behaviour symptoms ii) met clinical diagnostic criteria for MDD. The prevalence at each assessment point for both is shown in table 3.

Table 3 about here

Compared to BPI, the proportion of patients receiving an established psychological treatment (CBT+STPP) had significantly lower self reported ASB at 36 week assessment (Adj. diff -12.8% , 95% c.i. -23.8% to -1.9% ,p=0.022) but no significant difference by end of study (p=0.389).

There were no significant group differences for the proportion of patients in diagnostic remission by 36, 52 or 86 weeks. As this is a pragmatic study with no control group we compared the proportion in remission at 12 weeks with the proportion of remitted patients from the published TADS study randomised to a pill placebo control group (n=111) and also assessed at 12 weeks which gave: 145 (48%) of 305 patients compared to 37 (34%) of 111 pill placebo patients. [3] Additionally the treatment trial of resistant depression in adolescents, reported 61% in diagnostic remission by 72 weeks compared with 78% by the 86 week follow up in this study.[29] Finally15 (11%) patients relapsed by end of study from the 140 in remission at 36 and reassessed at 86 weeks (BPI= 5(11.6%)/48, CBT= 4(16.5%)/49, STPP 2 (4%)/48 STPP, p=0.149). Caution is required with these results: the study was not powered for treatment group comparisons, there are missing interview data at each time point and the control comparison could only be achieved at 12 weeks.

**Suicide Attempts and non-suicidal self injury**
Over the follow up period the proportion of patients who reported recent suicide attempts at each re-assessment point were: 36 week = 3 (3%)/279, 52 week = 2 (6%) /201, 86 week = 0/205 compared to 12 (3%)/465 at baseline. Similarly NSSI attempts were: 36 week = 19(7%)/268; 52 week= 14(4%)/234; 86 week= 16(5%)/257 which compares favourably with baseline = 85 (18%)/465 patients.

**Adverse effects of treatment**
There are no standardised methods for measuring the adverse effects of psychological treatments given to depressed adolescents. We derived a physical adversities score from self-reported items of breathing problems, sleep disturbances, drowsiness/tiredness, nausea, sweating, and being restless/overactive rated present/absent. Results are shown in table 4: there is a decline in the self reporting of adverse physical events over the course of the study with no observable differences between treatment groups.

**Cost-Effectiveness**
The cost of the trial interventions was: CBT (£904·57), BPI (£1292·91) and STPP (£1396·72). Use of all other services by 86-weeks differed little between groups: total costs = BPI (£1368·04), CBT ( £1459·26) STPP (£1668·51) (see appendix ii & iii). Including the cost of the trial interventions increased total costs per participant: BPI (£2678·39), CBT (£2379·01), STPP (£3081·70) respectively. There were no significant differences in these costs between treatment groups and no significant differences in QALYs (BPI group 1·241, CBT group 1·228 and STPP 1·246 QALYS over the 86 week follow up). There is no evidence to support the superior cost-effectiveness of STPP compared to BPI or CBT, nor of CBT compared to BPI (see appendix ii &iii for details).

**Discussion**
This trial found no evidence for the superiority of Cognitive Behaviour Therapy (CBT) or Short Term Psychoanalytic Therapy (STPP), compared to a brief psychosocial intervention (BPI), for maintaining reduced depression symptoms by end of study. This is the first trial to show that STPP and BPI are as clinically effective as CBT for the treatment of adolescent depression. We note the continuing decline of symptoms and further increase in remission, which are not explained by any marked differences in post-treatment service use, costs between therapies or reported SSRI use. We also note that there was a small reduction in symptoms in favour of established treatments at the end (36 weeks) of treatment but not by end of study, which is consistent with prior reports of psychological treatment effects on reducing anxiety in depressed patients.[30] There was no increase in suicidality, non-suicidal self-injury or adverse physical side effects in any therapy group over the study.

Three previous randomised controlled trials similar in design report follow up data beyond end of treatment. Birmaher and colleagues reassessed 107 adolescents with MDD two years after being treated with cognitive behavioral therapy, systemic behavioral family therapy, or nondirective supportive therapy. They reported no differences in outcome by original treatment group.[31] A naturalistic follow up study of 190 (44·6%, 89 of the original sample) depressed adolescents recruited to a treatment trial reported that five years post- trial recurrence was more likely in those with higher depressive symptoms at the end of treatment but was not associated with treatment type. [32] Most recently a 6 year follow up of a cognitive behaviour programme (CBP) aimed at preventing depressive episodes noted the strongest effect was early and maintained better with additional booster sessions and treatment of parental depression. [33] Overall these findings are consistent with suggesting early response to treatment can be followed by continued improvement across

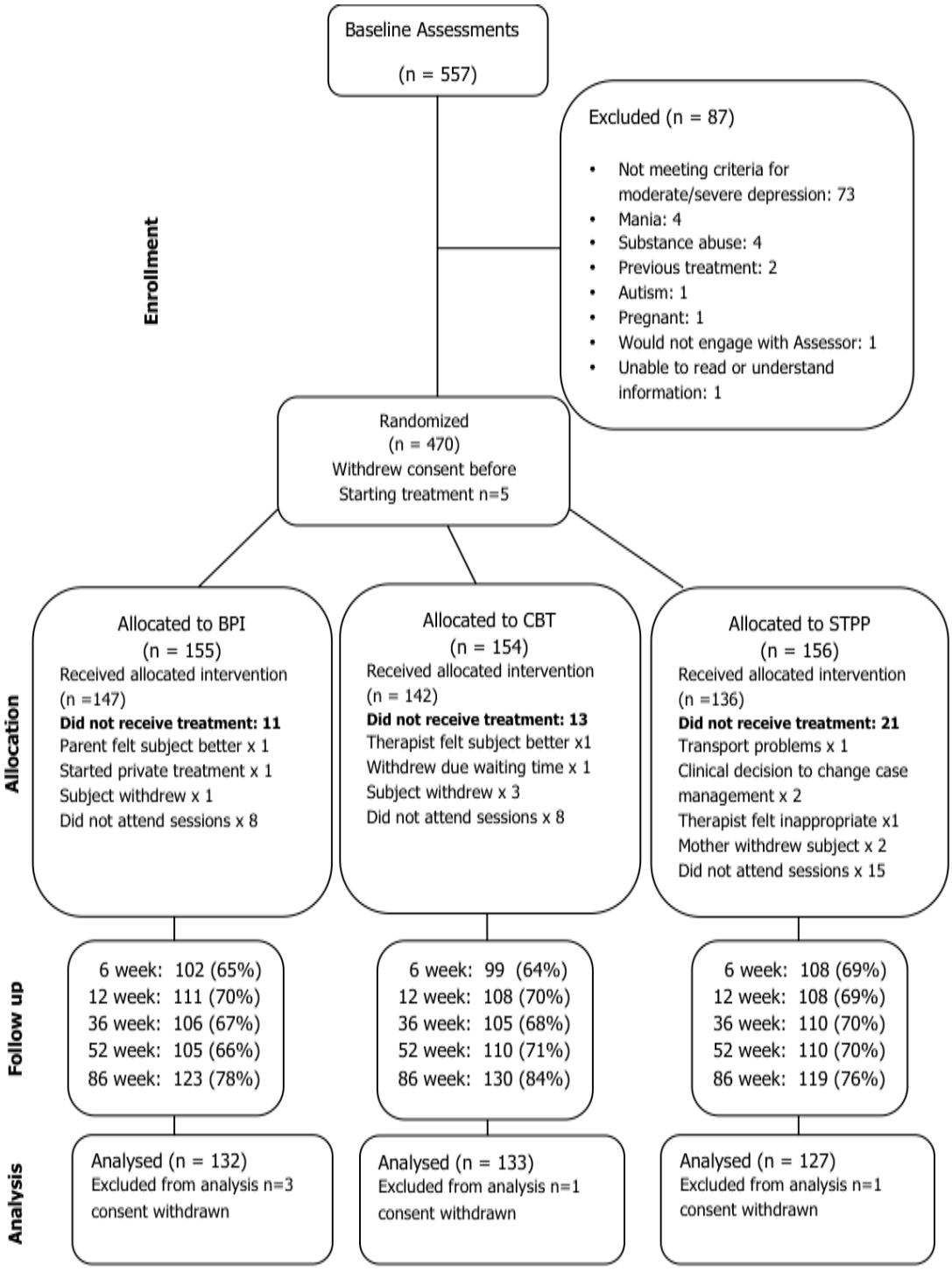
different treatment modalities. The lack of difference between these three treatments suggests there may be due to a putative shared common effect but there are alternative explanations including 3 unique effects leading to the same outcome and even no effect with the decline in symptoms being due to change over time.

There are also reports of non-response to treatment in 21-25% of trial patients consistent with these results.[3,10,29,30,31] This may be an issue of selecting the right treatment for the right patient, noting the likelihood of resistance to a given treatment early in therapy, or predicting the likelihood of non-compliance. One challenge for further research is to improve the precision of our ability to select the best therapy for a given depressed adolescent from the available treatment options. Despite the planned differences in treatment intensity, in practice young people attended a median of six to eleven sessions over 25-28 weeks across all three treatment arms. A first course of therapy for depressed adolescents could be brief (6-11 sessions) and at no difference in cost between the available treatment options evaluated in this trial. The reasons for non-attendance deserve further investigation.

This study had many strengths including that participants were representative of moderate to severe depression with self-harm, suicidality, and non depressive comorbid disorders at point of referral, referred to CAMHS across diverse regions of the UK, all met research diagnostic criteria for DSM IV Major Depressive Disorder, randomised remotely from the research team. There was a loss to follow up but the primary outcome measure (MFQ) was available in 84% of those randomised over the follow up period. The overall sample size was greater than prior studies and this is the first time a trial of depressed adolescents has designed to follow-up for 52 weeks after end of treatment. Each of the three treatments was manualised, therapies were delivered as expected and clear differences in approach were maintained between them. Some patients in all three groups received antidepressant medication. This characteristic strengthens generalisability but limits the interpretation of the findings. There were no prescribing difference between arms over the study and fluoxetine was prescribed both during and after the end of treatment. Neither the reasons for prescribing nor medication compliance were controlled for over the study course. We cannot therefore exclude the possibility that SSRIs may have contributed to the improvements over time. Furthermore the observed declines in symptoms and improvements in well-being could be a function of time. The absence of a no treatment control group limits the assertion that any therapy was causally effective. The economic results were limited by missing data, which was higher than for the primary clinical outcome measure (40%). Multiple imputation of missing data did not however change the economic results of the analysis. Future research should focus on psychological mechanisms associated with: treatment response, the maintenance of positive effects, non-response, and whether or not brief psychotherapies are of utility in community and primary care settings.

We conclude that all three treatments are associated with maintenance of reduced depressive symptoms a year after the end of treatment. STPP and BPI offers additional patient choice, alongside CBT for depressed adolescents attending routine specialist CAMHS.

**Figure 1**




The primary hypothesis was analysed with 392 (84%), of 465 who were randomised, accepted treatment and provided one or more self reported depression symptom score over the 36,52 or 86 week notional assessment points. Of these 39 (10%) had just one, 90 (23.0%) had two and 269 (67%) all three assessments scheduled.

**Table 1: Characteristics of participants at baseline**

| | BPI (N=155) | CBT (N=154) | STPP (N=156) |
|---|---|---|---|
| **Demographics** | | | |
| Mean Age in Years (range) | 15 (11-17) | 15 (12-17) | 15 (11-17) |
| Females | 115 (74%) | 114 (74%) | 119 (76%) |
| White* | 121 (82%) | 131 (86%) | 130 (86%) |
| **Stratification Variables** | | | |
| East Anglia | 61 (39%) | 62 (40%) | 62 (40%) |
| North London | 43 (28%) | 41 (27%) | 43 (27%) |
| North West | 51 (33%) | 51 (33%) | 51 (33%) |
| Conduct/Oppositional Disorder | 20 (13%) | 20 (13%) | 16 (10%) |
| Mean (SD) self-reported depression score | 46·2 (10·6) | 46·2 (10·3) | 45·4(10·8) |
| **Psychiatric Characteristics at Randomisation** | | | |
| Mean number of Interviewer assessed depressive symptoms | 8·4 (2·5) | 8·7 (2·3) | 8·3 (2·5) |
| SSRI prescribed before trial entry + | 29 (19%) | 32 (21%) | 28 (18%) |
| Prevalence of 1 or more comorbid DSM-V axis 1 psychiatric diagnoses | 71(46%) | 80(52%) | 74 (47%) |
| One or more Recent Suicide Attempts^ | 3 (2%) | 2(1%) | 7 (5%) |
| Lifetime Suicide Attempts | 57 (37%) | 48(31%) | 55 (35%) |
| Recent Self Harm Attempts^ | 26 (17%) | 25(16%) | 34 (22%) |
| One Or More Lifetime Non Suicidal Self Injury Episodes | 87 (56%) | 75(49%) | 84 (54%) |
| **Quality of Life at Randomisation** | | | |
| Mean (sd) HoNOSCA scores | 18·9 (6·0) | 18·4(6·0) | 18·3 (6·3) |
| Mean (sd) EQ5D scores | 0·596 (0·27) | 0·578 (0·58) | 0·569 (0·59) |

*excludes n=15 where ethnic group/origin was not stated or missing
+excludes n=9 with missing information
^ last 2 weeks

**Table 2: Mean outcome by treatment group over the trial for primary outcome and secondary outcomes**

| Assessment | BPI | | | CBT | | | STPP | | | Hypoth. | Weeks | Treatment Effect[a] | (95% C.I.) | p-value[b] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | n | Mean | SD | n | Mean | SD | n | | | | | |
| *Primary* | | | | | | | | | | | | | | |
| **MFQ[a]** | | | | | | | | | | | | | | |
| Baseline | 46.2 | 10.6 | 155 | 46.2 | 10.3 | 154 | 45.4 | 10.8 | 156 | STPP | 36 | 0.179 | (-3.731 to 4.088) | 0.929 |
| 6 week | 36.5 | 14.3 | 99 | 35.2 | 11.3 | 104 | 34.9 | 13.2 | 107 | vs. CBT | 52 | 0.307 | ( -3.161 to 3.774) | 0.862 |
| 12 week | 34.1 | 14.4 | 112 | 31.6 | 13.3 | 106 | 33.1 | 14.2 | 108 | | 86 | 0.578 | ( -2.948 to 4.104) | 0.748 |
| 36 week | 30.5 | 16.1 | 105 | 24.2 | 15.1 | 104 | 26.6 | 15.7 | 109 | (CBT+STPP) | 36 | -3.234 | (-6.611 to 0.143) | 0.061 |
| 52 week | 25.1 | 16.2 | 105 | 25 | 18.0 | 111 | 23.0 | 15.9 | 110 | vs BPI | 52 | -2.806 | (-5.790 to 0.177) | 0.065 |
| 86 week | 23.6 | 16.2 | 116 | 22.3 | 15.7 | 123 | 21.8 | 15.5 | 114 | | 86 | -1.898 | (-4.922 to 1.126) | 0.219 |
| *Secondary* | | | | | | | | | | | | | | |
| **RCMAS[a]** | | | | | | | | | | | | | | |
| Baseline | 41.1 | 7.6 | 155 | 41.2 | 6.4 | 154 | 40.5 | 7.7 | 155 | STPP | 36 | 0.855 | (-2.530 to 4.239) | 0.621 |
| 6 week | 35.9 | 10.6 | 98 | 37.1 | 7.9 | 103 | 36.7 | 10 | 107 | vs. CBT | 52 | 0.663 | (-2.354 to 3.680) | 0.667 |
| 12 week | 34.2 | 11.9 | 110 | 34.4 | 11.4 | 105 | 34.3 | 11.9 | 108 | | 86 | 0.254 | (-2.980 to 3.489) | 0.878 |
| 36 week | 32 | 13.3 | 104 | 27 | 13.7 | 102 | 28.6 | 13.3 | 107 | (CBT+STPP) | 36 | -3.832 | (-6.781 to -0.884) | 0.011 |
| 52 week | 27.2 | 14.8 | 100 | 26.4 | 14.9 | 108 | 25.5 | 14.5 | 104 | vs BPI | 52 | -2.818 | (-5.432 to -0.205) | 0.035 |
| 86 week | 24.7 | 14.7 | 109 | 24.8 | 15.4 | 115 | 23.8 | 14.6 | 108 | | 86 | -0.663 | (-3.460 to 2.134) | 0.642 |
| **LOI[a]** | | | | | | | | | | | | | | |
| Baseline | 10.0 | 5.3 | 155 | 10.8 | 5.4 | 152 | 9.2 | 5.0 | 154 | CBT vs STPP | 36 | -0.816 | (-1.972 to 0.341) | 0.167 |
| 6 weeks | 7.8 | 5.4 | 98 | 7.6 | 5.0 | 102 | 7.6 | 5.0 | 107 | | 52 | -0.574 | (-1.601 to 0.452) | 0.273 |
| 12 weeks | 6.6 | 5.6 | 111 | 6.7 | 5.2 | 104 | 7.3 | 5.1 | 107 | | 86 | -0.062 | (-1.091 to 0.967) | 0.906 |
| 36 weeks | 6.3 | 5.4 | 103 | 4.8 | 4.8 | 101 | 5.2 | 4.9 | 107 | | | | | |
| 52 weeks | 5.6 | 5.8 | 99 | 5.1 | 5.5 | 107 | 4.9 | 4.7 | 102 | (CBT+STPP) vs BPI | 36 | -1.249 | (-2.258 to -0.240) | 0.015 |
| 86weeks | 5.0 | 5.4 | 107 | 4.9 | 5.0 | 115 | 4.0 | 4.6 | 106 | | 52 | -1.120 | (-2.010 to -0.231) | 0.014 |
| | | | | | | | | | | | 86 | -0.847 | (-1.736 to 0 .042) | 0.062 |
| **HoNOSCA[a]** | | | | | | | | | | | | | | |
| Baseline | 18.9 | 6.0 | 148 | 18.4 | 6 | 143 | 18.2 | 6.3 | 144 | STPP | 36 | 0.617 | (-1.499 to 2.733) | 0.567 |
| 6 week | 14.5 | 6.5 | 88 | 14.1 | 6.4 | 91 | 14.6 | 6.9 | 96 | vs. CBT | 52 | 0.620 | (-1.078 to 2.318) | 0.474 |
| 12 week | 14.3 | 7.5 | 101 | 11.9 | 6.8 | 96 | 12.9 | 6.2 | 94 | | 86 | 0.626 | (-0.814 to 2.066) | 0.394 |
| 36 week | 12 | 8.7 | 88 | 9.7 | 7.2 | 81 | 10.3 | 7.6 | 88 | (CBT+STPP) | 36 | -1.410 | (-3.221 to 0.401) | 0.127 |
| 52 week | 9.5 | 6.9 | 88 | 8.5 | 7.3 | 86 | 8.6 | 5.8 | 83 | vs BPI | 52 | -1.154 | (-2.601 to 0.293) | 0.118 |
| 86 week | 8.2 | 6.2 | 98 | 7.3 | 5.2 | 92 | 8.2 | 7.2 | 85 | | 86 | -0.611 | (-1.819 to 0.598) | 0.322 |

[a] Linear Mixed Model estimates of the treatment effect at 36, 52, and 86 week post randomisation. Model based on data from 392 (84%), of 465 patients who provided one or more self reported depression symptom score over the 36,52 or 86 week notional assessment points. The analysis used time since randomisation as a continuous variable with therapist, participant and slope random effects, treatment, treatment by time interaction, and other pre-specified baseline covariates (see appendix).
Treatment effect is the marginal mean difference at time point with negative effects indicating treatment benefit.
Missing MFQ data at each assessment by group: 36 week, BPI 32%, 50 ; CBT 32%, 50 ; STPP 30%, 47 ; 52 week, BPI 32%, 50; CBT 28%, 43 ; STPP 29%, 46; 86 week 25%, 39 ; CBT 20%, 31 ; STPP 27%, 42.
**MFQ**: Mood and Feelings Questionnaire; **RCMAS**: Revised Children's Manifest Anxiety Scale**; LOI**: Leyton Obsessional Inventory-Adolescent version **HoNOSCA**: Health of the Nation Outcome Scale for Children and Participants

**Table 3: Proportion of Patients with MDD Diagnosis and One or more Antisocial Behaviour Symptoms (ABQ)**

| Assessment | BPI (N=155) | | | CBT (N=154) | | | STPP (N=156) | | | *Hypoth. | Weeks | Treatment Effect[a] | (95% C.I.) | p-value[b] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Total | (%) | N | Total | (%) | N | Total | (%) | | | | | |
| **MDD+** | | | | | | | | | | | | | | |
| Baseline | 155 | 155 | (100) | 154 | 154 | (100) | 156 | 156 | (100) | STPP | 36 | -0.064 | (-0.206 to 0.078) | 0.375 |
| 6 week | 63 | 143 | (99) | 57 | 95 | (60) | 62 | 99 | (63) | vs. CBT | 52 | -0.018 | (-0.120 to 0.084) | 0.727 |
| 12 week | 57 | 105 | (54) | 46 | 98 | (47) | 54 | 99 | (54) | | 86 | 0.057 | (-0.043 to 0.157) | 0.261 |
| 36 week | 42 | 95 | (44) | 28 | 89 | (31) | 35 | 98 | (36) | (CBT+STPP) | 36 | -0.043 | (-0.160 to 0.073) | 0.465 |
| 52 week | 27 | 92 | (29) | 23 | 90 | (26) | 23 | 87 | (26) | vs BPI | 52 | -0.053 | (-0.142 to 0.035) | 0.239 |
| 86 week | 27 | 99 | (27) | 24 | 95 | (25) | 14 | 92 | (15) | | 86 | -0.065 | (-0.152 to 0.022) | 0.145 |
| **ABQ** | | | | | | | | | | | | | | |
| Baseline | 121 | 155 | (78) | 124 | 152 | (81.6) | 128 | 154 | (83.1) | STPP | 36 | -0.068 | (-0.186 to 0.051)) | 0.263 |
| 6 week | 75 | 98 | (76) | 71 | 102 | (69.6) | 73 | 107 | (68.2) | vs. CBT | 52 | -0.040 | (-0.135 to 0.055) | 0.408 |
| 12 week | 78 | 111 | (70) | 57 | 104 | (54.8) | 52 | 107 | (48.6) | | 86 | 0.018 | (-0.083 to 0.120) | 0.725 |
| 36 week | 62 | 103 | (60.2) | 45 | 101 | (44.6) | 55 | 107 | (51.4) | (CBT+STPP) | 36 | -0.128 | (-0.238 to -0.019) | 0.022 |
| 52 week | 47 | 99 | (47.5) | 43 | 107 | (40.2) | 41 | 102 | (40.2) | vs BPI | 52 | -0.074 | (-0.163 to 0.015) | 0.102 |
| 86 week | 39 | 107 | (36.4) | 49 | 115 | (42.6) | 43 | 106 | (40.6) | | 86 | 0.040 | (-0.051 to 0.131) | 0.389 |

*Logistic GEE of the treatment effect at 36, 52, and 86 weeks post randomisation. Model based on data from 36 weeks post-randomisation with therapist, participant and slope random effects, treatment, treatment by time interaction, and other pre-specified baseline covariates ( or SAP. Treatment effect is the marginal mean difference at time point with negative effects indicating treatment benefit.
+This study was not powered to test for treatment differences in clinical diagnostic relapse and these results must be viewed with caution..
**MDD:** Major Depressive Disorder ; **ABQ**: Antisocial Behaviour Questionnaire.

**Table 4:** Summary statistics for adverse event score based on 6 adverse event items at each assessment

| Assessment | BPI* | | | | | | CBT* | | | | | | STPP* | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean | SD | Med | Min | Max | n | Mean | SD | Med | Min | Max | n | Mean | SD | Med | Min | Max |
| Baseline | 155 | 5.0 | 1.1 | 5 | 1 | 6 | 154 | 5.1 | 1.0 | 5 | 2 | 6 | 156 | 5.0 | 1.1 | 5 | 2 | 6 |
| 6 weeks | 99 | 4.4 | 1.5 | 5 | 0 | 6 | 104 | 4.6 | 1.3 | 5 | 2 | 6 | 107 | 4.4 | 1.5 | 5 | 0 | 6 |
| 12 weeks | 112 | 4.2 | 1.6 | 4 | 0 | 6 | 106 | 4.0 | 1.5 | 4 | 0 | 6 | 108 | 4.2 | 1.6 | 4 | 0 | 6 |
| 36 weeks | 105 | 4.1 | 1.6 | 4 | 0 | 6 | 104 | 3.6 | 1.6 | 4 | 0 | 6 | 109 | 3.6 | 1.7 | 4 | 0 | 6 |
| 52 weeks | 105 | 3.5 | 1.8 | 3.5 | 0 | 6 | 111 | 3.5 | 1.9 | 4 | 0 | 6 | 110 | 3.2 | 1.9 | 3 | 0 | 6 |
| 86 weeks | 116 | 3.3 | 1.8 | 3.5 | 0 | 6 | 123 | 3.4 | 1.9 | 4 | 0 | 6 | 114 | 3.2 | 1.8 | 3 | 0 | 6 |

* Sample size at each time point varies and is given in detail in table 3 above. The total sample size for each notional assessment period was baseline 465(100%); 6 week=310,67%,12 week= 326,70%, 36week = 318,68%, 52 week = 326, 70%, 86 week = 353, 76%. table

**Contributors**
IG, PF, SR, SB, MT, RK, BD, JH, CR, MR were responsible for the original proposal, securing funding, for the trial and drafting the original protocol. IG as chief investigator had overall responsibility for the management of the study. SR,RK and IG had responsibility for the East Anglia site, JH, BD for the North West site and RS,NM,MT and PF for the North London site. RK, BD, PW, IG were responsible for the development of the BPI manual and provided training and supervision for the therapists in East Anglia. Medical leadership and supervision for BPI was provided by RK in East Anglia, RS in North London and BD and JH in the North West. NM, MT, PF developed the STPP manual and ensured and coordinated STPP therapists for the study together with JH in the North West. SR developed the CBT manual, coordinated the therapists election, training and supervision for the study, BD and JH coordinated CBT therapy in the North West. BW was project manager throughout the trial, developed and coordinated the randomisation and minimisation protocol with IG and CR. BW set up and co-ordinated the database with all data held in a single repository on the Cambridge site. NM, SR, RK and BD coordinated and supervised the treatment fidelity project and analysed the data with CR. FH, CR, BB and SB wrote the statistical analysis plan and conducted the analyses. BW and FH were responsible for data cleaning. IG wrote the initial draft of the manuscript. All authors contributed to and approved the final manuscript.

**Declaration of Interests**
All authors have declare no competing interests.

**Acknowledgments**
This research was funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) programme (project number: 06/05/01). The views expressed in this publication are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS, or the Department of Health. The funding body had no role in the study design, patient recruitment, data collection, analysis or writing of the study, any aspect pertinent to the study or decision to submit to the Lancet.

The chief investigator has not been paid to write this article, has had full access to all the data in the study and has fhad inal responsibility for the decision to submit for publication.

We thank all the CAMHS practitioners who took part in this research and Laura Villis for her administrative support throughout. We also thank the specialist therapist who gave their professional time to rate audio tapes as experts.

1. Whiteford HA, Degenhardt L, Rehm J, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. Lancet 2013; 382(9904): 1575-86.
2. Cox GR1, Fisher CA, De Silva S, et al (2012) Phelan M, Akinwale OP, Simmons MB, Hetrick SE. Interventions for preventing relapse and recurrence of a depressive disorder in children and adolescents. Cochrane Database Syst Rev; 14;11:CD007504.
3. March J, Silva S, Petrycki S, et al. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. JAMA 2004; 292: 807-20.
4. Rush AJ, Wisniewski SR, Zisook S, et al. Is prior course of illness relevant to acute or longer-term outcomes in depressed out-patients? A STAR*D report. Psychological medicine 2012; 42: 1131-49.
5. National Institute of Clinical Excellence. CG28: Depression in children and young people: Identification and management in primary, community and secondary care. In: Excellence NIfHaC, editor.: National Institute for Health and Care Excellence; 2005.
6. Clarke K, Mayo-Wilson E, Kenny J, et al. Can non-pharmacological interventions prevent relapse in adults who have recovered from depression? A systematic review and meta-analysis of randomised controlled trials. Clin Psychol Rev 2015: 39:58-70.
7. Connolly Gibbons, M. B., Gallop, R., et al (2016). Comparative Effectiveness of Cognitive Therapy and Dynamic Psychotherapy for Major Depressive Disorder in a Community Mental Health Setting: A Randomized Clinical Noninferiority Trial. *JAMA Psychiatry*. 2016.1720
8. Abbass A, Rabung S, Leichsenring F, et al (2013). Psychodynamic Psychotherapy for Children and Adolescents: A Meta-analysis of short-term psychodynamic models. J Am Acad Child Adolesc Psychiatry, 52, 863-75.
9. Trowell J, Joffe I, Campbell J, et al. Childhood depression: a place for psychotherapy. An outcome study comparing individual psychodynamic psychotherapy and family therapy. Eur Child Adolesc Psychiatry 2007; 16(3): 157-67.
10. Goodyer I, Dubicka B, Wilkinson P, et al. Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behaviour therapy in adolescents with major depression: randomised controlled trial. BMJ 2007; 335(7611): 142.
11. Goodyer IM, Tsancheva S, Byford S, et al. Improving mood with psychoanalytic and cognitive therapies (IMPACT): a pragmatic effectiveness superiority trial to investigate whether specialised psychological treatment reduces the risk for relapse in adolescents with moderate to severe unipolar depression: study protocol for a randomised controlled trial. Trials 2011; 12: 175.
12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Washington,DC.: American Psychiatry Association 2000.
13. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Med 2010; 7(3): e1000251.
14. Daviss WB, Birmaher B, Melhem NA, Axelson DA, Michaels SM, Brent DA. Criterion validity of the Mood and Feelings Questionnaire for depressive episodes in clinic and non-clinic subjects. J Child Psychol Psychiatry 2006; 47(9): 927-34.
15. Gowers SG, Harrington RC, Whitton A, et al. Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA). Glossary for HoNOSCA score sheet. Br J Psychiatry 1999; 174: 428-31.
16. Bamber D, Tamplin A, Park RJ, et al (2002) Development of a short leyton obsessional inventory for children and adolescents. *J Am Acad Child Adolesc Psychiatry* 2002;**41**:1246-52
17. Reynolds CR, Richmond BO. What I Think and Feel: a revised measure of Children's Manifest Anxiety. J Abnorm Child Psychol 1997; 25(1): 15-20.
18. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 1997; 36(7): 980-8.
19. Posner K, Brown GK, Stanley B, et al. The Columbia–Suicide Severity Rating Scale: Initial Validity and Internal Consistency Findings From Three Multisite Studies With Adolescents and Adults Am J Psychiatry. 2011 Dec; 168(12): 1266–1277.
20. Vrouva I1, Fonagy P, Fearon PR, Roussow T. The risk-taking and self-harm inventory for adolescents: development and psychometric evaluation. Psychol Assess. 2010 Dec;22(4):852-65.
21. Hilsenroth MJ, Blagys MD, Ackerman SJ, Bonge DR, Blais MA. Measuring Psychodynamic-Interpersonal and Cognitive-Behavioral Techniques: Development of the Comparative Psychotherapy Process Scale. Psychotherapy: Theory, Research, Practice, Training, 2005; 42(3): 340-56.

22. Byford S, Barrett B, Roberts C, et al. Cost-effectiveness of selective serotonin reuptake inhibitors and routine specialist care with and without cognitive behavioural therapy in adolescents with major depression. The British Journal of Psychiatry 2007; 191: 521-7.
23. Byford S. The validity and responsiveness of the EQ-5D measure of health-related quality of life in an adolescent population with persistent major depression. J Ment Health 2013; 22(2): 101-10.
24. Graham P, Reynolds S, editors. Cognitive Behaviour Therapy for Children and Families. 3 ed. Cambridge: Cambridge University Press; 2015.
25. Walwyn R, Roberts C. Therapist variation within randomised trials of psychotherapy: implications for precision, internal and external validity. *Stat Methods Med Res* 2010; **19**(3): 291-315.
26. Byford S, Barrett B, Roberts C, et al. Cost-effectiveness of selective serotonin reuptake inhibitors and routine specialist care with and without cognitive behavioural therapy in adolescents with major depression. The British Journal of Psychiatry 2007; 191: 521-7.
27. National Institute of Clinical Excellence *Guide to the methods of technology appraisal* 2013; NICE, London.
28. Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. Health Econ 2001; 10(8): 779-87.
29. Vitiello B1, Emslie G, Clarke G, et al Long-term outcome of adolescent depression initially resistant to selective serotonin reuptake inhibitor treatment: a follow-up study of the TORDIA sample. J Clin Psychiatry. 2011 Mar;72(3):388-96.
30. Weisz JR, McCarty CA, Valeri SM. Effects of psychotherapy for depression in children and adoles- cents: A meta-analysis. . Psychological Bulletin 2008; 132 132– 49.
31. Birmaher B, Brent DA, Kolko D, et al. Clinical outcome after short-term psychotherapy for adolescents with major depressive disorder. Arch Gen Psychiatry 2000; 57(1): 29-36.
32. Curry J, Silva S, Rohde P, et al. Recovery and recurrence following treatment for adolescent major depression. Arch Gen Psychiatry 2011; 68(3): 263-9.
33. Brent, David A; Brunwasser, Steven M; Hollon, et al. (2016) Effect of a cognitive-behavioral prevention program on depression 6 years after implementation among at-risk adolescents: A randomized clinical trial. JAMA Psychiatry; 72(11): 1110-1118.